## REMARKS/ARGUMENTS

Claims 1-8 are pending in the present application. Claim 1 is slightly amended for better format. No new matter is added. Reconsideration of the present application is respectfully solicited in view of the following remarks.

In the final Office Action dated October 23, 2009, claims 1-8 stand rejected under 35 U.S.C. § 103 as unpatentable over Dolitzky et al. (WO 02/45658) in view of Rameshchandra et al. (WO03/050074). [1] In response, on January 6, 2010, Applicants submitted an Amendment in response to the final Office Action. Nevertheless, in the Advisory Action dated January 22, 2010, the Examiner maintains the rejections in the Final Office Action.

Applicants maintain and incorporate here the reasons discussed in the Amendment filed on January 6, 2010. The following are submitted to respond to the Examiner's statements set forth in the Advisory Action dated January 22, 2010.

First, in response to Applicants' comments responsive to the Final Office Action, the Examiner states "The thrust of said arguments is that the prior art relied upon teach that that the venlafaxine base is isolated prior to reacting with acid, while the instant claims do not require an isolation." Applicants disagree.

Independent claim 1 recites a process for preparing an acid addition salt of venlafaxine which comprises, among other things, (a) converting a venlafaxine precursor to venlafaxine in an aqueous solution; (b) extracting venlafaxine from the aqueous solution with a water-immiscible organic solvent to obtain **an** organic venlafaxine **solution**; and (c) reacting **the** organic venlafaxine **solution** with an acid to prepare the acid addition salt of venlafaxine.

As explained in the previously submitted response to the Final Office Action, based on the above bold language, claim 1 clearly reflects that the acid addition salt of venlafaxine is prepared by directly reacting a solution of venlafaxine with an acid in an organic solvent, which solvent is previously used for extracting venlafaxine from an aqueous reaction solution. In other words, according to claim 1, no step of isolating a solid or residue venlafaxine base from an organic phase, which is previously obtained during the

[1] Dolitzkyl is identified in the Office Action as WO 00/45658, which Applicants believe should be WO 02/45658 listed in Applicants' previously submitted IDS. Similarly, Rameshchandra is identified in the Office Action as WO 02/050074, which Applicants believe should be WO 03/050074 listed in Applicants' previously submitted IDS. Neither of the references as literally identified by the Office Action appears to be relevant to the present application. Should Applicants' assumption herein for facilitating the prosecution is incorrect, Applicants respectfully request that these two references be correctly identified.

extracting step, is conducted. The same water immiscible organic solvent used in the extracting step is also present in the subsequent step of reacting venlafaxine base with an acid.

Nevertheless, the Examiner again ignores the above-discussed limitations of claim 1 in the Advisory Action and therefore fails to identify any disclosure in Dolitzky or Rameschandra that discloses these limitations. Should the Examiner intend to maintain his present interpretation of the claims of the present application in the subsequent Office Action, Applicants respectively request that the Examiner call the undersigned to discuss the claims of the present application in distinguishing from the art of record.

Indeed, neither Dolitzky nor Rameschandra discloses the limitations discussed above in connection with the claims of the present application. The two references cited by the Examiner both actually teach away from the method of claim 1 of the present application.

Specifically, unlike the present invention, Dolitzky discloses that prior to the reaction with an acid to make a venlafaxine salt, solid venlafaxine base should be first isolated from an organic solution by evaporating an organic solvent that is contained therein and previously used for extracting the venlafaxine based from an aqueous reaction solution. *See*, for example, page 6, lines 12-24, Examples 1, 2, and 13. Although the ultimately produced venlafaxine salt of Dolitzky has sufficient purity, one would not conclude that the step of isolating venlafaxine base from the extracting organic phase should be omitted. On the contrary, one would reasonably conclude that the isolation step is essential and cannot be omitted to obtain a final acid salt of venlafaxine product with a satisfactory purity.

Similarly, the other reference Rameschandra also discloses that pure solid venlafaxine base should be used for making venlafaxine hydrochloride. *See* page 8, lines 1-2. Nowhere does Rameschandra teach reacting a venlafaxine solution, which contains a water immiscible organic solvent that is previously used to extract venlafaxine from the reaction solution, with an acid to prepare the acid addition salt of venlafaxine, as described in claim 1 of the present application. Moreover, because Rameschandra discloses that pure solid venlafaxine base should be used, which is expected to have a high purity, one would not expect success of reacting a venlafaxine base, which is not isolated from an organic solvent previously used for extracting venlafaxine from a reaction solution, with an acid. In other words, Rameschandra teaches away from the method of claim 1.

Indeed, in *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994), the Federal Circuit states that a prior art reference, which included a broad generic formula that encompassed the claimed composition, "appears to teach away from the selection of" the claimed composition "by focusing

on [fifteen] more complex" examples. Here, similarly, both references cited by the Examiner, Dolitzky and Rameschandra teach away from the present invention by disclosing a more complex process that requires first isolating venlafaxine base from a solution prior to reacting with an acid. In other words, a person of ordinary skill in the art would understand from Dolitzky and Rameshchandra that a simpler process that omit an isolating step would not work, because otherwise Dolitzky and Rameshchandra would have taught the simpler process.

Therefore, combining Dolitzky and Rameschandra, as proposed by the Examiner, would not have arrived at the method of claim 1 or any of its dependent claims 2-8 of the present application. For at least this reason, claims 1-8 are not obvious under 35 U.S.C. § 103 over Dolitzky in view of Rameshchandra.

The Examiner also comments that an artisan would have found it obvious to directly add an acid to a solution containing venlafaxine, without first isolation of the free base. Nevertheless, the Examiner does not articulate any objective reason that it would have been obvious for a person of ordinary skill in the art to do so. See MPEP2143.01 ("A statement that modifications of the prior art to meet the claimed invention would have been 'well within the ordinary skill of the art at the time the claimed invention was made' because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references."; "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art.")

As stated above, both Dolitzky and Rameshchandra teach and focus on a complex process by requiring the isolation of venlafaxine base prior to reacting velafaxine with an acid. Therefore, both Dolitzky and Rameshchandra teach away from the present invention. Neither Dolitzky nor Rameshchandra provides any reason to omit the step of isolating velafaxine base from a solution; nor does Dolitzky or Rameshchandra provide any reasonable expectation of success (e.g., obtaining a venlafaxine salt with satisfactory purity) to do so. In other words, the fact that a velafaxine salt product with a sufficient high purity can be obtained in accordance with the process of the present application which does not isolating venlafaxine base from a solution would not have been expected by a person of ordinary skill in the art. The HPLC purity of the venlafaxine hydrochloride obtained in each of Examples 2-3 of the present application, which are embodiments of the present invention, is 99.65 area%. Such unexpected results of the present invention further indicate that the claims of the present application are not obvious over the art of record.

Indeed, MPEP2144.04II.B explicitly states, "Omission of an Element with Retention of the Element's Function Is an Indicia of Unobviousness." (Quoting *In re Edge*, 359 F.2d 896, 149 USPQ 556 (CCPA 1966) (Claims at issue were directed to a printed sheet having a thin layer of erasable metal bonded directly to the sheet wherein said thin layer obscured the original print until removal by erasure. The prior art disclosed a similar printed sheet which further comprised an intermediate transparent and erasure-proof protecting layer which prevented erasure of the printing when the top layer was erased. The claims were found unobvious over the prior art because although the transparent layer of the prior art was eliminated, the function of the transparent layer was retained since appellant's metal layer could be erased without erasing the printed indicia.))

Moreover, as explained in our previous response, the primary reference Dolitzky discloses the use of water miscible solvent acetone or isopropyl alcohol during the converting reaction of venlafaxine to venlafaxine hydrochloride. *See* page 4, lines 1-4 and Figure 10. Although the secondary reference Rameshchandra mentions the possibility of adding a **water immiscible solvent** during the reaction of a pure solid venlafaxine with an acid, it does not provide any reason why a water immiscible solvent is preferable to a water miscible solvent. Neither Dolitzky or Rameshanda provides any reason why one should replace the water miscible solvent taught in the primary reference Dolitzky should be replaced with a water immiscible solvent; nor does the Examiner identify any objective reason to do so, as required by the relevant law. Indeed, in this aspect, the teachings of Dolitzky and Rameshanda are contradictory to each other and therefore are not combinable.

Additionally, the Examiner fails to realize that, according to claim 1 of the present application, the water immiscible solvent present during the reaction of venlafaxine solution with an acid is not newly added but comes from the previous step of extracting venlafaxine base. Rameshchandra by no means teaches that the water immiscible solvent used during the reaction of venlafaxine base with an acid derives from the previous step of extracting venlafaxine base from an aqueous reaction solution. Therefore, Rameshchandra cannot properly remedy the deficiency of Dolitzky.

Based on the foregoing, claims 1-8 are not obvious over Dolitzky and Rameshandra under 35 U.S.C. § 103. It is respectfully requested that the rejection of claims 1-8 be withdrawn.

It is believed that the present application is in a condition for allowance, early notice of which is earnestly solicited.

If any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
COHEN PONTANI LIEBERMAN & PAVANE LLP

By /Kent H. Cheng/
Kent H. Cheng
Reg. No. 33,849
551 Fifth Avenue, Suite 1210
New York, New York 10176
(212) 687-2770

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